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Length of storage of red blood cells does not affect outcome in critically ill children

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Sir: Length of red blood cell (RBC) storage has been proposed a contributing factor to adverse outcome after RBC transfusion. This may be explained by an impaired ability to transport or deliver oxygen, or the presence of leukocytes in stored RBC preparations producing potential deleterious pro-inflammatory mediators or bioactive lipids [1]. We hypothesized that length of RBC storage might explain our previously observed independent association

between RBC transfusion and increased mortality, duration of mechanical ventilation (MV) and length of paediatric intensive care unit (PICU) stay in critically ill children [2].

For each time a patient was transfused in our previous study, length of RBC storage was retrieved from our hospital's blood bank [2]. Since we observed a dose-outcome relation between the number of RBC transfusions and mortality, we separately looked at single transfusion and multiple transfusions. The effect of RBC transfusion on oxygenation was assessed by the oxygenation index (OI, mean airway pressure times FiO_2 divided by PaO_2) and $\text{PaO}_2/\text{FiO}_2$ ratio. RBC preparations were leukocyte-depleted, but not irradiated. Statistical analysis was performed using the Student *t*-test; linear regression analysis was applied to study correlations. $P < 0.05$ was accepted as statistically significant.

Data of 295 patients were studied, of whom 67 (22.7%) were transfused; 39 (58.2%) were transfused only once, the remaining 28 received multiple transfusions at different time

intervals (range 2–14) (Table 1). Seventeen (5.8%) patients died. The mean length of RBC storage was 16.7 ± 0.6 days [25–75% interquartile range (IQR) 9–23 days]. Length of RBC storage was comparable between survivors and non-survivors. This remained after comparing single versus multiple transfusions. Differences in OI and $\text{PaO}_2/\text{FiO}_2$ ratio between the first day and fifth day after transfusion, duration of MV and length of PICU stay were not correlated with length of RBC storage.

Our findings indicate that our previously reported observed independent association between transfusion of leukocyte-depleted RBC preparations and increased morbidity in critically ill children could not be explained by length of RBC storage. Mortality was also not influenced by length of RBC storage, although our study might not be powered to detect this. To our knowledge, although the issue of RBC transfusion has been extensively studied in critically ill adults, no other paediatric data on length of RBC storage and outcome in critically ill children have been reported. Results from retrospective and prospective

Table 1 Effect of length of red blood cell storage on oxygenation and patient outcome

	Single transfusion (<i>N</i> = 39)		Multiple transfusions (<i>N</i> = 28)		
Mean length of RBC storage (days ± SEM)	14.6 ± 1.3 (25–75% IQR 7–20 days)		15.9 ± 1.4 (25–75% IQR 8–23 days)		
Effect of length of RBC storage on oxygenation					
	<i>R</i> ²	<i>P</i> value	<i>R</i> ²	<i>P</i> value	
ΔOI day 1 to day 5	0.036	0.684	<0.001	0.995	
ΔPaO ₂ /FiO ₂ day 1 to day 5	0.340	0.169	0.025	0.517	
Effect of length of RBC storage on patient outcome					
Duration of ventilation	0.002	0.830	0.177	0.065	
Length of PICU stay	0.001	0.827	0.047	0.268	
Effect of length of RBC storage on mortality					
	Survivors (<i>N</i> = 35)		Non-survivors (<i>N</i> = 4)	Survivors (<i>N</i> = 21)	Non-survivors (<i>N</i> = 7)
Mean length of RBC storage (days ± SEM)	14.7 ± 1.4		13.5 ± 3.0	15.8 ± 1.5	16.0 ± 3.5
<i>ΔOI</i> difference in oxygenation index, <i>ΔPaO₂/FiO₂</i> difference in PaO ₂ /FiO ₂ ratio, <i>RBC</i> red blood cell, <i>SEM</i> standard error of the mean					

ΔOI difference in oxygenation index, $\Delta\text{PaO}_2/\text{FiO}_2$ difference in $\text{PaO}_2/\text{FiO}_2$ ratio, RBC red blood cell, SEM standard error of the mean

observational studies on the association between RBC storage and outcome in critically ill adults are difficult to interpret as they yield conflicting results [1, 3]. The outcome of (some of) these studies are probably confounded by a lack of transfusion policy and the use of leukocyte-non-depleted RBC preparations. Our observations on lack of correlation between change in oxygenation, duration of MV or PICU stay and length of RBC storage are compatible with experimental and clinical data indicating no difference in regional or global indexes of tissue oxygenation, or patient outcome in critically ill adults with organ failure [4–6].

Despite the limitations of our study (relatively small number of patients, single-center retrospective study and lack of transfusion algorithm), we conclude that no association between length of RBC storage and patient outcome could be demonstrated in our patient population. A prospective randomized trial comparing “fresh”

versus “old” blood in critically ill (paediatric) patients seems warranted.

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